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Relationship between serum lipid concentrations and posttraumatic stress symptoms in the bereaved after the Sewol ferry disaster: A prospective cohort study

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ABSTRACT

The objective of this study was to investigate the relationship between serum lipid concentrations and PTSD symptoms in the bereaved after a traumatic familial loss. Eighteen months after the Sewol ferry disaster, 107 subjects who experienced traumatic losses as a result of the accident completed a mental and medical survey as well as laboratory tests for lipid profiles. At 30 months after the trauma, a total of 64 individuals completed a follow-up psychometric survey and biochemical measurements. We performed multiple linear regression analyses, examining the association between PTSD symptoms and lipid profiles. Other potential influences on lipid profiles such as metabolic risk factors, demographic risk factors, and underlying medical history were accounted for. Participants reporting clinically significant PTSD symptoms exhibited lower serum HDL-C levels than those without PTSD symptoms. In addition, we found that the severity of PTSD symptoms and sex could explain the changes in lipid profiles independently of other possible risk factors of changes. The results of this study suggest that PTSD symptoms may contribute to an increased risk for developing metabolic syndrome via detrimental changes in lipid concentrations. Routine screening and multidisciplinary management to prevent metabolic syndrome in individuals who experience traumatic losses would therefore be valuable.

1. Introduction

Previous studies have reported changes in serum lipid concentrations in patients with mental disorders (Boston et al., 1996). Hypercholesterolemia has been reported in patients with schizophrenia, obsessive-compulsive disorder, panic disorder, and generalized anxiety disorder (Bajwa et al., 1992; Jakovljevic et al., 2007). Low concentrations of cholesterol have been reported in patients with major depressive disorder, dissociative disorder, antisocial personality disorder, and borderline personality disorder (Agargun et al., 2004; Atmaca et al., 2002; New et al., 1999; Olusi and Fido, 1996; Rabe-Jablonska and Poprawska, 2000). Other studies have reported lower high-density lipoprotein (HDL-C) levels (Lehto et al., 2010) and lower HDL-cholesterol to total cholesterol ratios in patients with major depressive disorder compared with controls (Maes et al., 1997; Vilibić et al., 2014).

Among psychiatric disorders, there is also evidence that posttraumatic stress disorder (PTSD) is associated with metabolic syndrome (Jakovljevic et al., 2006; Violanti et al., 2006) including being overweight (David et al., 2004; Vieweg et al., 2007), obese, and dyslipidemic (David et al., 2004; Jin et al., 2009; Maia et al., 2008). A study that included Croatian veterans with combat-related PTSD found higher total cholesterol, triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) concentrations as well as a lower LDL-C to HDL-C ratio compared with veterans without PTSD (Karlovic et al., 2004). Similarly, Kagan et al. (1999) in their pioneer study, as well as some investigators recently (Džubur Kulenović, et al., 2008; Vilibić et al., 2014) found that combat-related PTSD is accompanied with elevated total cholesterol, LDL-C, and TG levels as well as reduced HDL-C levels. Maia et al. (2008) also reported that people with PTSD exhibited higher serum total cholesterol, LDL-C, and TG levels than those without PTSD.

PTSD symptoms may develop when a traumatic event causes an over-reactive adrenergic response, which can have a deep neurophysiological impact on the brain. During traumatic experiences, high levels of secreted stress hormones suppress hypothalamic activity, which may be a major factor in the development of PTSD (Zohar et al., 2008). Some studies have described different biological alterations in patients with PTSD such as increased noradrenergic activity (Southwick et al., 1999) and hyper-regulation of the hypothalamic-pituitary-

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adrenocortical (HPA) axis (Thaller et al., 1999). The correlation between stressful situations and increased serum lipids is also due to biological changes; these alterations are sometimes used as biological stress markers in people with PTSD (Southwick et al., 1999).

The aim of this study was to analyze the relationship between serum lipid concentrations and PTSD symptoms in the bereaved after a traumatic familial loss. Three sets of hypotheses were tested: (1) individuals in the PTSD group would exhibit abnormal serum lipid profiles, especially HDL-C; (2) more abnormal lipid concentrations would manifest in individuals with more severe PTSD symptoms; and (3) the severity of PTSD symptoms would be associated with the extent of changes in lipid concentrations independently of other possible variables of changes. To the best our knowledge, this is the first study to analyze the relationship between PTSD symptoms and lipid profiles using follow-up data from subjects who suffered the same traumatic event. We expected that individuals with severe PTSD symptoms would have lower HDL-C than those with less severe PTSD symptoms.

2. Methods

2.1. Participants and procedures

The data used in this study are from the disaster cohort study on mental health problems in disaster-affected people, especially the bereaved victims of the Sewol ferry disaster. The Sewol ferry disaster was an unexpected accident in which the ship capsized and sank in the southwestern Sea of Korea on April 16, 2014. Out of 476 passengers and crew members, 304 people died in the disaster. A total of 339 passengers were sophomore students and teachers from Danwon High School who were on a field trip, and 261 students and teachers from the school died. Most of the bereaved were deeply affected by this unexpected traumatic loss and they appeared to suffer from complicated grief and posttraumatic stress symptoms. The study examining mental health of the bereaved families was registered to the cohort study of the Korean Mental Health Technology R&D Project, Ministry of Health & Welfare. Participants of this study were recruited with cooperation from the Ansan Mental Health Trauma Center after obtaining an agreement from representatives of the bereaved families. The center contacted 516 bereaved family members to ask if they wanted to participate in the study, and a total of 107 participants were initially recruited (Fig. 1). The surveys were scheduled, and the questionnaires were disseminated through the center. The exclusion criteria were: (a) a previous or current diagnosis of any psychiatric disorder with psychotic features, bipolar disorder, or substance use disorder; (b) any history of significant head injury defined as an external injury to the brain resulting in loss of consciousness for at least 10 min; (c) more than two family members from each family; (d) underlying dyslipidemia; and (e) use of medications which could affect lipid measurements, including psychotropic medications.

The mental and medical health questionnaires were administered to participants at the beginning of the study and during the follow-up survey. The first baseline survey and biochemical measurements were performed 18 months (SD = 1 month) after the accident. Venous blood samples were collected immediately following the interview. All 107 individuals recruited for the study completed the mental and medical survey, and participated in blood sample collection for baseline biochemical analysis. After 12 months of follow-up (30 months after the accident), a total of 64 individuals completed the survey and participated in biochemical analysis.

The investigation was carried out in accordance with the latest version of the Declaration of Helsinki. This study was approved by the [removed for blind review]. Written informed consent was obtained from all subjects after providing them with a complete description of the study.

2.2. Measurements

The PTSD Checklist-5 (PCL-5), a screening instrument for PTSD, was used to assess posttraumatic symptoms related to the Sewol ferry disaster. The PCL-5 is a 20-item self-reporting tool that assesses the DSM-5 subcategorical symptoms of PTSD, including intrusion, avoidance, negative alterations in cognition and mood, and arousal and reactivity. Each item is rated on a 5-point Likert scale based on the degree to which a participant has been impacted by the trauma. PCL-5 scores are summed to yield a continuous measure of PTSD severity for symptom clusters and for the disorder as a whole. A preliminary validation study suggested a cutoff score of 38 for PTSD screening (Hoge et al., 2014); for the present study, we used the same cutoff value. As a screening tool for PTSD, the PCL-5 has demonstrated excellent reliability and validity (Blevins et al., 2015).

Alcohol problems were assessed using the Alcohol Use Disorders Identification Test-Alcohol Consumption questionnaire (AUDIT-C) (Bush et al., 1998). The AUDIT-C is rapidly becoming the preferred alcohol screening test for busy practitioners (Khadjesari et al., 2017); it is a 3-item alcohol screening test to identify persons who are hazardous drinkers or have an active alcohol use disorder. Responses are rated using a 5-point Likert scale, yielding a total score ranging from 0 to 12. Total scores can be interpreted as the absence of an alcohol problem (0–7), problem drinking (8–10), or alcohol dependence (11–12) (Bradley et al., 2003).

All participants completed the questionnaires that included basic demographic characteristic and medical history, including hypertension, diabetes mellitus, cerebrovascular disease, acute or chronic physical illness, and medication use. Tobacco consumption was also evaluated during the interview, and participants were asked about their amount of daily tobacco use before and after the accident. Participants were also asked to complete a smoking history checklist, including non-smoking periods.

Height, weight, and blood pressure were measured and recorded, and body mass index (BMI, kg/m^2) was calculated for all participants. Blood samples for the chemistry panel, including fasting plasma glucose, HbA1C, and the lipid panel (total cholesterol, HDL-C, LDL-C, TG), were drawn in the morning. Blood samples were collected from a forearm vein in a glass red-topped vacuum tubes without anticoagulant and centrifuged at 3000 rpm for 15 min. Sera were separated from the clots and stored at $-20\,^{\circ}C$ until analysis. An Olympus AU 2700 analyzer was used to measure TG, HDL-C, LDL-C, and total cholesterol levels using an enzymatic method.

2.3. Data analysis

Two-tailed tests were used in all instances, and statistical significance was defined by $p < .05$ with confidence intervals at 95%. Participants were categorized into PTSD or non-PTSD groups based on the PCL-5 scores at baseline. An independent samples t test was used to examine differences in lipid concentrations (serum HDL-C, LDL-C, TG, and total cholesterol) between the PTSD and non-PTSD groups. In addition, the relationship between PTSD symptoms (PCL-5 total score and subscale scores) and serum cholesterol levels (HDL-C, LDL-C, TG, and total cholesterol) were examined as continuous variables using the Pearson correlation coefficient.

Finally, we examined whether PTSD symptoms were associated with follow-up serum HDL-C concentrations when controlling for variables having possibilities to affect cholesterol levels. Multiple linear regression models were performed to evaluate whether PTSD is the independent risk factor for lipid imbalance. One possible explanation for confounders is that subjects with a history of PTSD may be prone to dyslipidemia due to metabolic or demographic factors associated with the disease. Table 4 lists three sets of potential confounders based upon the three different hypotheses: 1) lipid levels were due to baseline data (age, sex, and BMI); 2) lipid levels were due to substance use (alcohol